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FIG.1

CCGGGTCGACCCACCGTCCGAAGGCCCCCTCACTCCGCTCCACTCCTCGGGCTGG
5 CTCTCCTGAGGATGCACCAGCGTCACCCCCGGCAAGATGCCCTCCCTGTGTGGC
CGGAATCCTTGCTGTGGCTTCTCCTGGCTGCTGGGACCCCTCCATTCCAGCAGA
GTTGTCTCAGGCTTGGAGCCACAGGCCGTGTCTTACTTGAGCCCTGGTGTCCC
TTAAAAGGCCGCCCTCCTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCCGG
CTGCAGGCCGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCGATGTCTTCA
10 GGCTCACCAAGGAGGACACAGAGCGCTATGTGCTACCAACCTAACATGGGGCAGAA
CTGCTTCGGGACCCGTCCCTGGGGCTCAGTTGGGTGCACCTGGTAAGATGGTCA
TTCTGACAGAGCCTGAGGGTGCTCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG
AGCGTCTGTGGTGGAGCCAGACCATCAACCTGAGGACGACACGGATCCTGGCCATG
CTGACCTGGTCCTCTATATCACTAGGTTGACCTGGAGTTGCCTGATGTAACCGGCAG
15 GTGCGGGCGTCACCCAGCTGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA
CCGAGGACACTGGCTTCGACCTGGAGTCACCATTGCCATGAGATTGGGCACAGCTT
CGGCCTGGAGCAGCACGGCGCGCCGGCAGCGGCTGCGGCCAGCGGACACGTGA
TGGCTTCGGACGGCGCCGCGCCCCCGGCCGCTGCCCTGGTCCCCCTGCAGCCGCC
GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGCGCCTGCGTGTGGACCCGCCGC
20 GGCCTCAACCCGGGTCCGGGGCACCGCCGGATGCGCAGCCTGGCTACTACA
GCGCCAACGAGCAGTCGGCTCGCCCTGGCCCTGGCCACAGACCCGCTGGACCAA
CAGGGAGCACCTGGATATGTGCCAGGCCCTCCTGCCACACAGACCCGCTGGACCAA
AGCAGCTGAGCCGCTCCCTCGTCCCTGGATGGACAGAAATGTGGCGTGGAGA
AGTGGTGTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCATAGCAGCAGT
25 GCATGGCGCTGGTAGCTGGGCCCCGAAGTCCTGCTCCGCTCCTGCAGGAGGA
GGTGTGGTACCAAGGAGGGCGAGTGCAACAACCCAGACCTGCCTTGGGGCGT
GCATGTGTTGGTGCCTGACCTCCAGGCCAGATGTGCAACACTCAGGCCTGCGAGAAGA
CCCAGCTGGAGTTATGTGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC
CTCCCCCTGGCGGCCCTCCTTACCAACTGGGTGCTGCTGTACACACAGCCAAGGG
30 GATGCTCTGTGAGACACATGTGCCGGCATTGGCAGAGAGCTTCATCATGAAGCGTG
GAGACAGCTCCTCGATGGGACCCGGTGTATGCCAAGTGGCCCCGGAGGACGGGA
CCCTGAGCCTGTGTGTGGCGAGCTGCAGGACATTGGCTGTGATGGTAGGATGGA
CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGGTGGGACAACAGCACGTGCAGC
CCACGGAAAGGGCTTTCACAGCTGGCAGAGCGAGAGAAATATGTCACGTTCTGACAGT
35 TACCCCCAACCTGACCAAGTGTCTACATTGCCAACACAGGCCTCTTACACACTTGG
CGGTGAGGATGGAGGGCGCTATGCGTGGCTGGGAAGATGAGCATCTCCCTAACAC
CACCTACCCCTCCCTGGAGGATGGCGTGTGAGTACAGAGTGGCCCTACCGAG

Substituted

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GACCGGGCTGCCCGCCTGGAGGAGATCCGCATCTGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTACAGGCCTATGGCAGGGAGTATGGCAACCTCACCGCCAGACA
TCACCTCACCTACTTCCAGCCTAACGCCACGGCAGGCCTGGGTGTGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGCAGGGCTGCCTGGTAAACTACAGCTGCCTG
5 GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTCGCTGCTGAACCCCTGCCCTCCCTACTGGCGGTGGGA
GACTTCGGCCCATGCAGCGCTCCTGTGGGGTGGCCTGCAGGGAGCCAGTGCCTG
TGCCTGGAGGCCAGGGCAGCCTCTGAAGACATTGCCCTCAGCCCAGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC
10 AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGCAGATGCCCTGGAGGCTCCAGTGACTGAGG
GCCCTGGCTCCGTAGATGAGAACGCTGCCCTGCCCTGAGCCCTGTGTGGATGTCATG
TCCTCCAGGCTGGGCCATCTGGATGCCACCTCTGCAGGGAGAACGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGCTCAAGCTGCACACGTGTGGACCCCTGCCAGGG
15 TCGTGTCCGTCTCCTGCAGGGCAGGTCTGATGGAGCTGCCTTGATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGCCCTGGCAAGCAAGCCTGGAG
CCGGCGGGAGGTCTGCCAGGCTGCCCTGCCCTGCTCGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGAGAGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGCT
20 GCCTGCCCGAACCCCCAGGAGGCCCTGCAGCCTGGAGCCCTGCCACCTAGGTGGAA
AGTCATGTCCTGGCCCATGTTGCCAGCTGTGCCCTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCCCTGT
GCGCGCTGGTGCAGGCCAGGCACTGTCCCCTGTCTATTGCCACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTCTGTGGGATGGCATCCAGCG
25 CCGGCGTGACACCTGCCCTGGACCCAGGCCAGGGCCCTGTGCCAGCTGATTCTGC
CAGCACTGCCCAAGCCGGTACTGTGCGTGGCTGCTGGCTGGCCCTGTGTGGAC
AGGGTACGCCAGCCTGGTCCCCACGAAGAACGCCCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCAGGGCAGGCAGACTGTGCAGTGGCATTGGCGGCCCTCGGGAGGT
30 GGTGACCCCTCCGCGTCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTCA
GCTCCAAGACCAACACGCTGGTGGTGGAGGCAGCGCTGCGGCCAGGAGGTGGGG
TGCTGCTGCCGTATGGAGGCCAGCTGCTCTGAAACCTCTACAGAGAATGTGACATG
CAGCTTTGGCCCTGGGTGAAATCGTGAGCCCCCTCGCTGAGTCCAGCCACGAGTA
35 ATGCAGGGGGCTGCCGGCTTCAATTAAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGCAGCAGGTGCTACTG

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GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCCTCCAATCATGGGTACCGGAGATGCAGGACC
CTCAGTCCTGGAAGGGAAAGGAAGGAACC

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FIG. 2

5

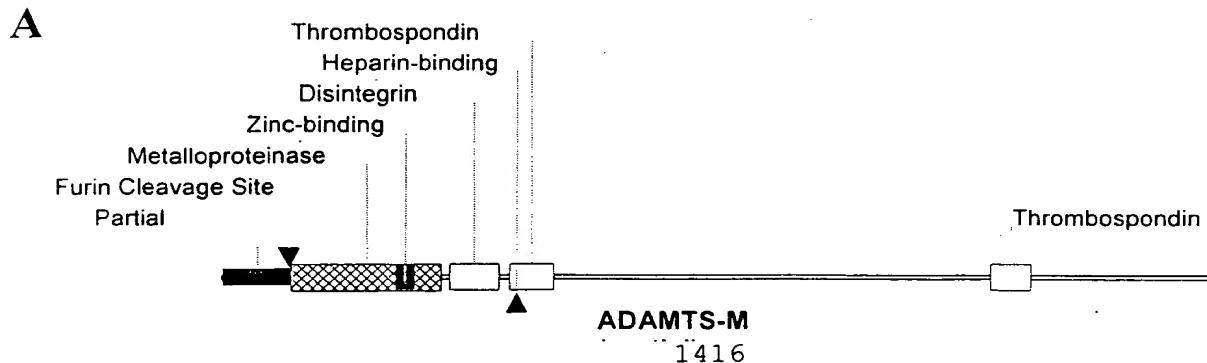
PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPHFQQSCL
QALEPQAVSSYLSGPAPLKRPPSPGFQRQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPDSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVQLGGACSPWSCLITEDTGFDLGVTIAHEI
10 GHSFGLHEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLVPLLDGTECGVEKWCSPKGRCRSLVELTPIAAVHGRWSSWGRSPCSRSCGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSCVS
15 GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVAGKMSISPNTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEETYGNLTRPDITFTYFQPKPRQAWWWAAVRGPPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPAWPEACVLEPCPPYWAvgDFGPPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQAQPAVALETCPQPCPARWEVSEPSCTSAGGAGLAL
20 ENETCVPGADGLEAPVTEGPGSVDEKLPAPPEPCVGMSCPPGWGHLDATSAKEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSDLRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVRRILYCARAHGEDDGEIILDTQCQGLPRPEPQE
ACSLPCPPRWKVMQLGPPCSASCGLGTARRSVACVQLDQGQDVVEDEAACAAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRTCLGPQAQAPVPADFCQHLPKPVTVRGC
25 WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCABAIGR
PLGEVVTLRVLESSLNCAGDMLLWGRLTWRKMCRKLLDMTFSSKTNTLVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

30

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Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) ADAMTS-M nucleotide sequence with translated amino acid sequence above.



B

```

+1 P G R P T R P K A P S H S A P L L G L A L L R M H Q R
                                         Partial Prodomain
=====
25 CCGGGTGCAC CCACCGCTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGACCCAGCG
GCCCGAGCTG GGTGCGCAGG CTTCCGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC
=====
+1 H P R A R C P P L C V A G I L A C G F L L G C W G F
                                         Partial Prodomain
=====
105 TCACCCCCGG GCAAGATGCC CTCCCCCTCTG TGTGGCCGG AATCCTTGCT GTGGCTTCT CCTGGGCTGC TGGGGACCCCT
AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACCGA CACCGAAAGA GGACCCGACG ACCCCTGGGA
=====
+1 S H F Q Q S C L Q A L E P Q A V S S Y L S P G A P L K
                                         Partial Prodomain
=====
185 CCCATTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
GGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAAC CGGGACCAAC AGGGAATTTC
=====
+1 G R P P S P G F Q R Q R Q R R A A G G I L H L E L
                                         Furin Cleavage Site (Motif)
=====
                                         Partial Prodomain
                                         Metalloproteinase Domain
=====
265 GGCCGCCCTC CTTCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
CGGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA
=====
+1 L V A V G P D V F Q A H Q E D T E R Y V L T N L N I
                                         Metalloproteinase Domain
=====
345 GCTGGTGGCC GTGGGCCCG ATGTCTTCCA GGCTCACCAAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
CGACCAACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
=====
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+1 G A E L L R D P S L G A Q F R V H L V K M V I L T E P
Metalloproteinase Domain
=====

425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGCAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA

+1 E G A P N I T A N L T S S L L S V C G W S Q T I N P E
Metalloproteinase Domain
=====

505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCCTGA
CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TC GGTC TGGT AGTTGGGACT

+1 D D T D P G H A D L V L Y I T R F D L E L P D G N R
Metalloproteinase Domain
=====

585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCTCTAT ATCACTAGGT TTGACCTGGA GTTGCTGTGAT GGTAACCCGGC
CCTGCTGTGC CTAGGACCCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG

+1 Q V R G V T Q L G G A C S P T W S C L I T E D T G F D
Metalloproteinase Domain
=====

665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCATTA CCGAGGACAC TGGCTTCGAC
TCCACGCCCG CCAGTGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCTGTG ACCGAAGCTG

+1 L G V T I A H E I G H S F G L E H D G A P G S G C G P
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCC
GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG

+1 S G H V M A S D G A A P R A G L A W S P C S R R Q L
Zinc-binding Motif
=====

Metalloproteinase Domain
=====

825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
GTCGCCTGTG CACTACCGAA GCCTGCCGCG CGCGGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCGTCGACG

+1 L S L L S A G R A R C V W D P P R P Q P G S A G H P P
Metalloproteinase Domain
=====

905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCCG GGTCCGCGGG GCACCCGCC
ACTCGGACGA GTCGCGTCCT GCCCGCGCGA CGCACACCCCT GGGCGGCCCG GGAGTTGGGC CCAGGCCGCC CGTGGCGGC

+1 D A Q P G L Y Y S A N E Q C R V A F G P K A V A C T F
Disintegrin Domain
=====

985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTGGCCCC AAGGCTGTG CCTGCACCTT
CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA

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+1 A R E H L D M C Q A L S C H T D P L D Q S S C S R L
Disintegrin Domain

=====

1065 CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGCTGG GCGACCTGGT TTCGTCGACG TCGGGAGGAG

+1 L V P L L D G T E C G V E K W C S K G R C R S L V E L
Disintegrin Domain

=====

1145 TCGTTCCCTC CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCCTC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTCCCAGCGA CGGCAGGGAGA CCACCTCGAC

+1 T P I A A V H G R W S S W G P R S P C S R S C G G G V
Heparin-binding Motif

=====

1225 ACCCCCCATAG CAGCAGTGCA TGGGCCTGG TCTAGCTGGG GTCCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
TGGGGGTATC GTCGTACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCCTCCACA

+1 V T R R R Q C N N P R P A F G G R A C V G A D L Q A
Thrombospondin Submotif

=====

1305 GGTCAACCAGG AGGCAGGAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGGCG
CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC

+1 E M C N T Q A C E K T Q L E F M S Q Q C A R T D G Q P
Thrombospondin Submotif

=====

1385 AGATGTGCAA CACTCAGGCC TGCAGAGAAGA CCCAGCTGGA GTTCATGTGCG CAACAGTGC CGAGGACCGA CGGCCAGCCG
TCTACACGT GTGAGTCCGG AGCCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTACAGC GGTCTGGCT GCCGGTCCGG

+1 L R S S P G G A S F Y H W G A A V P H S Q G D A L C R
1465 CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCA
GACGCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTACAGC CACGACGACA TGGTGCTGCG GTTCCCCTAC GAGACACGTC

+1 H M C R A I G E S F I M K R G D S F L D G T R C M P
1545 ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
TGTGTACACG GCCCCGTAAC CGCTCTCGA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATAACGGTT

+1 S G P R E D G T L S L C V S G S C R T F G C D G R M D
1625 GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTC GGGCAGCTGC AGGACATTG GCTGTGATGG TAGGATGGAC
CACCGGGGGC CCTCCTGCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG

+1 S Q Q V W D R C Q V C G G D N S T C S P R K G S F T A
1705 TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
AGGGTCTGTC ATACCCTGTC CACGGTCCAC ACACCACCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTG

+1 G R A R E Y V T F L T V T P N L T S V Y I A N H R P
1785 TGGCAGAGCG AGAGAATATG TCACGTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
ACCGTCTCGC TCTCTTATAC AGTCAAAGA CTGTCATGG GGGTTGGACT GGTACAGAT GTAACGGTTG GTGTCCGGAG

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+1 L F T H L A V R I G G R Y V V A G K M S I S P N T T Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCTAA CACCACTAC
AGAAGTGTGT GAACGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG

+1 P S L L E D G R V E Y R V A L T E D R L P R L E E I R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
GGGAGGGAGG ACCTCCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGCGGACCC TCCTCTAGGC

+1 I W G P L Q E D A D I Q V Y R R Y G E E Y G N L T R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGGGT ATGGCGAGGA GTATGGCAAC CTCACCCGC
GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCCG

+1 P D I T F T Y F Q P K P R Q A W V W A A V R G P C S V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCTGGGTG TGGCCGCTG TGCGTGGGCC CTGCTGGTG
GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC

+1 S C G A G L R W V N Y S C L D Q A R K E L V E T V Q C
2185 AGCTGTGGGG CAGGGCTGCG CTGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
TCGACACCCCC GTCCCGACGC GACCATTG ATGTCGACGG ACCTGGTCCG GTCCCTCCTC AACACACCTCT GACAGGTAC

+1 Q G S Q Q P P A W P E A C V L E P C P P Y W A V G D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGCG GTGGGAGACT
GGTCCCTCG GTCGTCGGTG GTCCGACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCCTCTGA

+1 F G P C S A S C G G G L R E R P V R C V E A Q G S L L
2345 TCGGCCCATG CAGCGCCTCC TGTTGGGGTG GCCTGCGGGA CGGCCAGTG CGCTGCGTGG AGGCCAGGG CAGCCTCTG
AGCCGGTAC GTCGCGAGG ACACCCCCAC CGGACCCCT CGCCGGTCAC GCGACGCACC TCCGGTCCC GTCGGAGGAC

+1 K T L P P A R C R A G A Q Q P A V A L E T C N P Q P C
2425 AAGACATTGC CCCCAGCCCG GTGAGAGCA GGGGCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
TTCTGTAACG GGGTCCGGC CACGTCTCGT CCCCCGGTCG TCGGTGACA CGCGACCTT TGGACGTTGG GGGTCCGGAC

+1 P A R W E V S E P S S C T S A G G A G L A L E N E T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCTTGGAG AACGAGACCT
GGGACGGTCC ACCCTCCACA GTCTCGGTC GAGTACGTGT AGTCGACCCAC CTCGTCCGGA CGCGACCTC TTGCTCTGGA

+1 C V P G A D G L E A P V T E G P G S V D E K L P A P E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGAATGAGA GGGGCTGGC TCCGTAGATG AGAAGCTGCC TGCCCTGAG
CACACGGTCC CGCTCTACCG GACCTCCGAG GTCACTGACT CCCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC

+1 P C V G M S C P P G W G H L D A T S A G E K A P S P W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGATGCCATC TGGATGCCAC CTCTGCGAGGG GAGAAGGCTC CCTCCCCATG
GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCGGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC

+1 G. S I R T G A Q A A H V W T P A A G S C S V S C G R
2745 GGGCAGCATIC AGGACGGGGG CTCAGCTGC ACACGTGTGG ACCCCTGCCG CAGGGCTGTG CTCCGTCTCC TGCGGGCGAG
CCCCGTCTAG TCCTGCCCTCC GAGTCGACG TGTCGACACC TGGGGACGCC GTCCAGCAC GAGGCAGAGG ACGCCCGCTC

+1 G L M E L R F L C M D S A L R V P V Q E E L C G L A S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCCTC TCGACACACC GGACCGTTCG

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+1 K P G S R R E V C Q A V P C P A R W Q Y K L A A C S V
2905 AAGCCTGGGA GCCGGCGGGA GGTCGCCAG GCTGCTCCGT GCCCTGCTCG GTGGCAGTAC AAAGCTGGCGG CCTGCAGCGT
TTCGGACCCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTGACCGCC GGACGTCGCA

+1 S C G R G V V R R I L Y C A R A H G E D D G E E I L
2985 GAGCTGTGGG AGAGGGGTCG TGGGGAGGAT CCTGTATTGT GCCCCGGGCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
CTCGACACCC TCTCCCCAGC ACGCCTCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA

+1 L D T Q C Q G L P R P E P Q E A C S L E P C P P R W K
3065 TGGACACCCA GTGCCAGGGG CTGCCCTGCC CGGAACCCCA GGAGGCCAGC AGCCTGGAGC CCTGCCACC TAGGTGGAAA
ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGT CCTCCGGACG TCGGACCTCG GGACGGGTGG ATCCACCTT

+1 V M S L G P C S A S C G L G T A R R S V A C V Q L D Q
3145 GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTGGTG GCTGTGTGC AGCTCGACCA
CACTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT

+1 G Q D V E V D E A A C A A L V R P E A S V P C L I A
3225 AGGCCAGGAC GTGGAGGTGG ACGAGGGCGGC CTGTGCGGCC CTGGTGGCGC CCGAGGCCAG TGTCCCCGT CTCATTGCCG
TCCGGTCCCTG CACCTCCACC TGCTCCGGC GACACGCCGC GACCACGGCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC

+1 D C T Y R W H V G T W M E C S V S C G D G I Q R R R D
Thrombospondin Submotif

=====
3305 ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTCC TGTGGGATG GCATCCAGCG CGGGCGTGAC
TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCGCGACTG

+1 T C L G P Q A Q A P V P A D F C Q H L P K P V T V R G
Thrombospondin Submotif

=====
3385 ACCTGCCTCG GACCCAGGC CCAGGCCTG GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCAC TAAAGACGGT CGTAGGACGGG TTCGGCCACT GACACGACCG

+1 C W A G P C V G Q G T P S L V P H E E A A A P G R T
Thrombospondin Submotif

=====
3465 CTGCTGGCT GGGCCCTGTG TGGGACAGGG TACGCCAGC CTGGTCCCC ACGAAGAACG CGCTGCTCCA GGACGGACCA
GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTCG GCGACGAGGT CCTGCCTGGT

+1 T A T P A G A C G R Q H L E P T G T I D M R G P G Q A
3545 CAGCCACCC TGCTGGTGC TGTCAGGC AGCACCTGA GCCAACAGGA ACCATTGACA TGCGAGGCC AGGGCAGGCA
GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGAACCT CGGTTGTCCT TGGTAACGT ACGCTCCGGG TCCCCTCCGGT

+1 D C A V A I G R P L G E V V T L R V L E S S L N C S A
3625 GACTGTGCAG TGGCCATTGG GCGGGCCCTC GGGGAGGTGG TGACCCCTCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
CTGACACGTC ACCGGTAACC CGCGGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCA

+1 G D M L L L W G R L T W R K M C R K L L D M T F S S
3705 GGGGGACATG TTGCTGCTT GGGGCCGGCT CACCTGGAGG AAGATGTCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
CCCCCTGTAC AACGACGAAA CCCGGCCGA GTGGACCTCC TTCTACACGT CCTCGACAA CCTGTACTGA AAGTCGAGGT

+1 K T N T L V V R Q R C G R P G G G V L L R Y G S Q L A
3785 AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
TCTGGTTGTG CGACCACAC TCCGTCGCGA CGGGCGCCGG TCCTCCACCC CACGACGACG CCATACCTC GGTCGAACGA

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+1 P E T F Y R E C D M Q L F G P W G E I V S P S L S P A
3865 CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTG GGCCCTGGGG TGAAATCGT AGCCCTCGC TGAGTCCAGC
GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAC CCGGGACCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTG

+1 T S N A G G C R L F I N V A P H A R I A I H A L A T
3945 CACGAGTAAT GCAGGGGGCT GCGGCTCTT CATTAAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
GTGCTCATTA CGTCCCCCGA CGGGCGAGAA GTAATTACAC CGAGGGGTGC GTGCCTAACG GTAGGTACGG GACCGGTG

+1 N M G A G T E G A N A S Y I L I R D T H S L R T T A F
4025 ACATGGGCAGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
TGTACCCCGG ACCCTGGCTC CCTCGTTAC GGTGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG

+1 H G Q Q V L Y W E S E S S Q A E M E F S E G F L K A Q
4105 CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTCAGC GAGGGCTTCC TGAAGGCTCA
GTACCCGTCG TCCACGAGAT GACCCCTAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT

+1 A S L R G Q Y W T L Q S W V P E M Q D P Q S W K G K
4185 GGCCAGCCTG CGGGGCCAGT ACTGGACCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GTTAGTACC CATGGCCTCT ACGTCCCTGGG AGTCAGGACC TTCCCTTCC

+1 E G T
4265 AAGGAACC
TTCCCTTCC

Fig. 4

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

		Percent Homology	
		Sim	Ident
hADAMTS-4 (AB014588)	(202) SPSPRR--	360	32
hADAMTS-5 (AF142099)	(241) QSLSPAGGGPQIWWBRARQ-	44	44
hADAMTS-1 (AF060152)	(220) QGVQQTGTGSI--	44	28
hADAMTS-8 (AF060153)	(199) ASEPPPIGAT-	47	29
hADAMTS-2 (AJ003125)	(248) EHANSRR--R--	46	29
M1-MPD	(1) -----	46	32
Consensus	P R KRPAS R VETLLVAD	49	32
hADAMTS-4 (AB014588)	(251) KAFKHEPFRNPVSYVTRVLTGSGEEPOYGP-SANOTLSEFCAORGNTPEEDDEDI	420	
hADAMTS-5 (AF142099)	(299) RYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK-		
hADAMTS-1 (AF060152)	(274) RYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK-		
hADAMTS-8 (AF060153)	(253) RYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK-		
hADAMTS-2 (AJ003125)	(300) RYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK-		
M1-MPD	(39) RYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK- KLYKHPATENHTRAWKVVWVGGDKDKLEVKSK-		
Consensus	(361) RLYKHPSTI N I LVVVK VIL D GPEV NAA TLRNFC WQ N P D HPEH	421	480
hADAMTS-4 (AB014588)	(310) I PAAVQ QDGGS VSTEEDY MADIGIV D AR AYEDD LQSNMIA	421	480
hADAMTS-5 (AF142099)	(358) V AVHQS EDCGG HHSEDEI MADIGIV D AR AYEDD LQSNMIA		
hADAMTS-1 (AF060152)	(333) V AVHQS EDCGG SODEDY MADIGIV D AR AYEDD LQSNMIA		
hADAMTS-8 (AF060153)	(312) V AVHQS ONEQGQGLD VADIGIV D AR AYEDD LQSNMIA		
hADAMTS-2 (AJ003125)	(360) H HADIGIV D QDEGP S--NO YEPVGM H AR AYEDD LQSNMIA		
M1-MPD	(98) A LVIYQE F DDELPDNRQYR VEQGGAA STW LKETD ED GYVII VQHSEG		
Consensus	(421) YDTAIIUTTRODLCG G CDTLGMDGT CDP RSC VIEEDGLOQAF T AHEIGHVLG	481	540
hADAMTS-4 (AB014588)	(369) YL NSKPOISINELSTSRN AYMMHVPEED E SARFIID D NGYGH E K		
hADAMTS-5 (AF142099)	(417) IS DSKTQETTFSSTE-DIEL SSILTSIDASKD K TSATIIE D DDEGDN D E		
hADAMTS-1 (AF060152)	(392) VP DAKQASTIN-VNOOSIN RSMISNLDSOQ E SRYMILIS D NGYGH E M E K		
hADAMTS-8 (AF060153)	(372) VP DSSPOTRLEFFPMEG-KHVAZLTVHLAQTE E SAVYIIE D GCHGDDTQAP		
hADAMTS-2 (AJ003125)	(416) YEN GQG --NRCDEVRLGSI ALVQQAHRHR V R SQQEISRLES-YD E D		
M1-MPD	(158) YEN GAP --GGCCESG --IV PWSGMAAPRAGLA E P SRRQILSISAGRAF V W P		
Consensus	(481) M HDDSK C SL GP HVMAS D PWSPCSA LT FLD GHG CLD P		

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541
nADAMTS-4 (AB014588)
nADAMTS-5 (AF142099)
nADAMTS-1 (AF060132)
nADAMTS-8 (AF060153)
nADAMTS-2 (AJ003125)
M1-MPD
Consensus
(541) A LP LPG YDA QC TFGPD HCP D CA LWC G C
RP

541
(429) EAP--LHEDVTEPG--KDYADRODQLEGPDSRICE--QLPPPCAAWESCHLNCHAMC
(476) RKO--ILGEEDPG--QDIDTQDNLEEGEYSEV--GMDTARLNGAVRQEDQWV
(451) QNP--IQEDSDPG--1SDDNRSGOFEGEDSKHCP--DAASTSTTNGCTSGJLV
(431) GNA--LPUBTCPEGRMAYOLDODORQIEGEDFRHCPITSAQDVAQDWH-TDGAEPIC
(471) FADWPALE-QIPG--LHMSMNEQRFDEGYMMCTAERTFDPEKQWGS-HPDNPYFC
(213) RP

600